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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,303	02/26/2004	Kelly Reed Clark	28335/40012	8089
4743 7590 04/25/2008 MARSHALL, GERSTEIN & BORUN LLP 233 S. WACKER DRIVE, SUITE 6300 SEARS TOWER CHICAGO, IL 60606			EXAMINER BURKHART, MICHAEL D	
			ART UNIT	PAPER NUMBER
			1633	
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			04/25/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/789,303

**Applicant(s)**

CLARK ET AL.

**Examiner**

Michael Burkhardt

**Art Unit**

1633

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 February 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-5, 8-14, 18, 19 and 21-38 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 8-14, 18, 19 and 21-38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Receipt and entry of the amendment dated 2/4/2008 is acknowledged. After entry of the amendment, claims 1-5, 8-14, 18, 19, and 21-38 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, and 22-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection necessitated by amendment of claim 1.**

Claim 1 recites the limitation "said rAAV-producing cell insert" in line 9. There is insufficient antecedent basis for this limitation in the claim. This rejection affects all dependent claims.

#### ***Claim Rejections - 35 USC § 102***

Claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Natsoulis et al (U.S. Patent 6,027,931, 2000). **This rejection is maintained for reasons made of record in previous Office Actions dated 7/9/2005, 4/4/2006, 12/20/2006, 8/3/2007, and for reasons set forth below.**

The claims have been amended to recite "said rAAV-producing cell insert has been modified to overexpress" Rep 52/40 proteins. The instant specification does not provide a definition for a cell insert, hence, a reasonably broad interpretation of the term includes insertion of vectors into cells, e.g. the vectors encoding Rep/Cap proteins taught by Natsoulis et al. Such vectors overexpress Rep52/40 proteins for reasons of record (reiterated below), and are considered to have been "modified": the pRCM.kozak was modified with the Kozak sequence, and pRCM.polyA was modified with polyadenylation site (see column 14, lines 44-50).

***Response to Arguments***

Applicant's arguments filed 2/4/2008 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) Natsoulis et al teach that the changes to the pRCM.kozak and pRCM.polyA vectors had "little effect on Rep protein expression" and do not state that the Rep52/40 proteins in Figure 2, lanes 4 and 5 demonstrate overexpression; 2) Natsoulis et al do not purposefully overexpress Rep52/40 as required by the instant claims; 3) claim 1 recites that the expression level of Rep 78/68 has not been genetically down-regulated, a limitation not taught by Natsoulis et al; 4) claims 3 and 10 require that the expression cassette be introduced subsequently to cells already comprising an AAV genome and rep-cap proteins, whereas Natsoulis et al teaches one transfection of one rep-cap construct in Example 1; 5) Natsoulis et al teach that an AAV helper vector comprises functions missing from the AAV vector, thus the sequential transfection taught by Natsoulis et al in column 12 is not a sequential transfection of rep-cap sequences; 6) claim 18 requires infection with a simian adenovirus, whereas Natsoulis et al clearly exclude adenovirus from the definition of an accessory function vector.

Regarding 1) and 2), the instant claims are broadly drawn to a range of Rep protein expression levels, particularly the levels of Rep 52/40 proteins. For example, claim 1 only requires that Rep 52/40 be overexpressed, without any limit as to the extent of overexpression relative to expression under control of the p19 promoter. Thus, a "little" overexpression is considered to meet this limitation of the claim. Natsoulis et al teaches overexpression of Rep 52/40 for reasons of record. Furthermore, there is no requirement that prior art actually state the claim limitations verbatim. There is little to no room to misinterpret the results of Fig. 2: there is more of the Rep 52/40 proteins in the relevant lanes (pRCM.kozak and pRCM.polyA) than in the control lane. This is all that is required to meet the claim limitation regarding Rep 52/40 overexpression. Finally, the intent or purpose of Natsoulis et al in making the modifications to the pRCM vector is irrelevant here. A review of 35 USC 102(b) reveals that there is no requirement that prior art teaching all the limitations of a product claim have the same intent or purpose as applicants.

Regarding 3), the claim limitation that the Rep 78/68 expression levels are not achieved by genetic down-regulation is a product-by-process limitation. Such claims are not limited by the process steps, but rather by the product implied by the steps. See MPEP §2113:

"If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

In this case, the prior art cells express levels of Rep 78/68 considered to at the level expressed by the p5 promoter for reasons made of record, and thus anticipate the instant claims. Further, because these expression levels are the same, it is unclear how the Rep 78/68 levels in the pRCM.kozak and poly A vectors could be considered "genetically down-regulated": they are simply not down-regulated at all.

Regarding 4) and 5), the teachings of Natsoulis et al are not limited to Example 1, or the first ¶ of column 7. To reiterate, the AAV vector and AAV helper function (i.e. the Rep/Cap constructs of Fig. 1) may be transfected into the cell sequentially (column 12, lines 39-42). The Rep 52/40 provided by the AAV helper constructs are considered "supplemental" to any encoded by the AAV vector. The AAV vector may include rep-cap coding sequences, column 6, last ¶. Such AAV vectors were known to the skilled artisan, see pPAK-CN in Fig. 1B of Fan et al (1997, of record). The teachings of Natsoulis et al in column 7 wherein the rep and cap genes are used to complement AAV functions missing from the AAV vectors does not rule out the situation set forth above.

Regarding 6), it is abundantly clear that Natsoulis et al do not exclude infection by adenoviruses as a means of providing accessory functions. See column 4, lines 20-24 and 28-30; the sentence linking column 7 and 8; and column 13 lines 46-54. The section cited by applicants teaches the exclusion of natural, or wild type, viruses, probably for safety reasons. As set forth previously, the claims are not limited to naturally occurring viruses, and it is noted that the adenoviruses used in the instant specification are not naturally occurring, but rather, are (at the least) E1-deleted and/or E3-deleted.

Finally, it is noted that the prior art of record does appear to teach or suggest adding a supplemental Rep52/40 expression cassette that does not also include Rep78/68 sequences. Although no currently pending claims are so limited, applicants appear to contemplate this situation (in the Summary of the Invention section) and provide recombinant adenoviruses that express Rep 52/40 and not Rep 78/68.

***Claim Rejections - 35 USC § 103***

Claims 22, 26, 28, 29, 31, 35, 37, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al (6,027,931) as applied to claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33 above, and further in view of Hardy (U.S. Patent 6,429,001, 2002).

Claims 25 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al (6,027,931) as applied to claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33 above, and further in view of Murphy (U.S. Patent 6,635,476, 2003, effective filing date of 10/15/1999).

Claims 27-29 and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al and Hardy as applied to claims 1-3, 10-13, 18, 21-24, 26, 28-33, 35, 37, and 38 above, and further in view of Potash et al (U.S. Patent 5,911,998, 1999).

Claims 4, 5, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al (6,027,931) as applied to claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33 above, and further in view of Collaco et al (Gene, 1999).

Claims 9, 14 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al (6,027,931) and Collaco et al (Gene, 1999) as applied to claims 1-5, 8, 10-13, 18, 21, 23, 24, 30, 32 and 33 above, and further in view of Gao et al (U.S. Patent 7,235,393, effective filing date 4/29/2002) and the ATCC entry for VR-199, i.e. Simian virus 20 (of record).

**These rejections are maintained for reasons made of record in the previous Office Actions dated 7/9/2005, 4/4/2006, 12/20/2006, 8/3/2007, and for reasons set forth below.**

***Response to Arguments***

Applicant's arguments filed 2/4/2008 have been fully considered but they are not persuasive. Because the arguments relating to the above 35 USC §103 rejections are essentially the same, they are addressed together. Applicants essentially assert that Natsoulis et al does not teach all the instant claim limitations, and the other documents cited above do not remedy the deficiency of Natsoulis et al. This is not persuasive because for reasons set forth above, Natsoulis et al is still considered anticipatory for claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33. Therefore, it is considered the above claims are rendered obvious as set forth above and as set forth in the previous Office Actions.

***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,



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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Burkhardt whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Weitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1633

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Primary Examiner, Art Unit 1633